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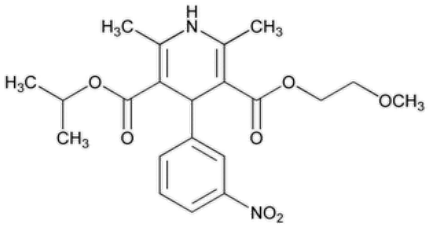
Nimodipine



$C_{21}H_{26}N_2O_7$ 418.44

3,5-Pyridinedicarboxylic acid, 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, 2-methoxyethyl 1-methylethyl ester;

Isopropyl 2-methoxyethyl 1,4-dihydro-2,6-dimethyl-4-(*m*-nitrophenyl)-3,5-pyridinedicarboxylate CAS RN®: 66085-59-4; UNII: 57WA9QZ5WH.

DEFINITION

Nimodipine contains NLT 98.0% and NMT 102.0% of nimodipine ($C_{21}H_{26}N_2O_7$), calculated on the dried basis.

[NOTE—Throughout the following procedures, protect samples, the Reference Standards, and solutions containing them by conducting the procedures without delay, under subdued light, or using low-actinic glassware.]

IDENTIFICATION

Change to read:

• **A.** ▲**SPECTROSCOPIC IDENTIFICATION TESTS ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-MAY-2020)

• **B.** The retention time of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **PROCEDURE**

Mobile phase: Methanol, tetrahydrofuran, and water (20:20:60)

Standard solution: 0.3 mg/mL of USP Nimodipine RS prepared as follows. Transfer a quantity of USP Nimodipine RS to a suitable volumetric flask, dissolve in a volume of tetrahydrofuran equivalent to 10% of the total volume, and dilute with *Mobile phase* to volume.

Sample solution: 0.3 mg/mL of Nimodipine prepared as follows. Transfer a quantity of Nimodipine to a suitable volumetric flask, dissolve in a volume of tetrahydrofuran equivalent to 10% of the total volume, and dilute with *Mobile phase* to volume.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 235 nm

Column: 4.6-mm × 12.5-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 2 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of nimodipine ($C_{21}H_{26}N_2O_7$) in the portion of Nimodipine taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of nimodipine from the *Sample solution*

r_S = peak response of nimodipine from the *Standard solution*

C_S = concentration of USP Nimodipine RS in the *Standard solution* (mg/mL)

C_U = concentration of Nimodipine in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Organic Impurities**

Mobile phase and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard stock solution A: 1.6 mg/mL of USP Nimodipine RS prepared as follows. Transfer a quantity of USP Nimodipine RS to a suitable volumetric flask, dissolve in a volume of tetrahydrofuran equivalent to 10% of the total volume, and dilute with *Mobile phase* to volume.

Standard stock solution B: 0.8 mg/mL each of USP Nimodipine RS and USP Nimodipine Related Compound A RS prepared as follows. Transfer quantities of USP Nimodipine RS and USP Nimodipine Related Compound A RS to a suitable volumetric flask, dissolve in a volume of tetrahydrofuran equivalent to 10% of the total volume, and dilute with *Mobile phase* to volume.

Standard solution A: 3.2 µg/mL of USP Nimodipine RS from *Standard stock solution A* in *Mobile phase*

Standard solution B: 1.6 µg/mL each of USP Nimodipine RS and USP Nimodipine Related Compound A RS from *Standard stock solution B* in *Mobile phase*

Sample solution: 1.6 mg/mL of Nimodipine prepared as follows. Dissolve 40 mg of Nimodipine in 2.5 mL of tetrahydrofuran, and dilute with *Mobile phase* to 25 mL.

System suitability

Sample: *Standard solution B*

[Note—The relative retention times for nimodipine related compound A and nimodipine are about 0.9 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between nimodipine related compound A and nimodipine

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution A*, *Standard solution B*, and *Sample solution*

Calculate the percentage of nimodipine related compound A in the portion of Nimodipine taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of nimodipine related compound A from the *Sample solution*

r_S = peak response of nimodipine related compound A from *Standard solution B*

C_S = concentration of USP Nimodipine Related Compound A RS in *Standard solution B* (µg/mL)

C_U = concentration of Nimodipine in the *Sample solution* (µg/mL)

Calculate the percentage of any other impurity in the portion of Nimodipine taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response of nimodipine from *Standard solution A*

C_S = concentration of USP Nimodipine RS in *Standard solution A* (µg/mL)

C_U = concentration of Nimodipine in the *Sample solution* (µg/mL)

Acceptance criteria

Nimodipine related compound A: NMT 0.1%

Any unspecified impurity: NMT 0.2%

Total impurities: NMT 0.5%

SPECIFIC TESTS

- **Optical Rotation** ⟨781S⟩, *Procedures, Specific Rotation*

  Sample solution: 50 mg/mL in acetone

  Acceptance criteria: −0.10° to +0.10°, at 20°

- **Loss on Drying** ⟨731⟩

  Analysis: Dry at 105° for 4 h.

  Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers, and store at controlled room temperature.
- **USP Reference Standards** ⟨11⟩

  USP Nimodipine RS

  USP Nimodipine Related Compound A RS

2-Methoxyethyl-1-methylethyl-2,6-dimethyl-4-(3-nitrophenyl)pyridine-3,5-dicarboxylate.

$C_{21}H_{24}N_2O_7$ 416.42

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
NIMODIPINE	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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